REMARKS

This responds to the Office Action mailed on December 6, 2005, and the references cited therewith.

Claims 59-106 are pending in this application. However, pursuant to the requirement for restriction, claims 59-73, 77 and 85-106 have been withdrawn from consideration by the Examiner. As a result, claims 74-76 and 78-84 are now under examination.

The term "is/are adapted to" has been added to claims 74 and 79. Applicant submits that this language is supported by the specification as filed, for example, at page 13, line 28 to page 14, line 3 and page 17, lines 1-11. Applicant submits that this change adds no new matter to the specification.

Pursuant to the Examiner's request, Figure 10 has been added to the specification and a description of Figure 10 has been inserted at page 9, line 3. Applicant submits that Figure 10 and its description merely illustrate an embodiment of the invention that was already clearly described by the specification as originally filed. In particular, the subject matter of Figure 10 and its description is clearly described in the specification, for example, at page 12, line 29 to page 17, line 17 (see especially, page 14, lines 4-29). Moreover, the subject matter of Figure 10 is embraced by presently pending Claims 74-84.

Applicant submits that these changes add no new matter to the application.

Objection to the Drawings

The Examiner has objected to drawings, stating that the sensor of claims 74-84 must be shown in a drawing or the features thereof canceled from the claims. Given that the objection to the drawings will not be held in abeyance and that the Examiner has threatened that the application will be abandoned if no drawing is submitted, Applicant has submitted Figure 10 and a description thereof with this response.

Applicant submits that submission of Figure 10 is not necessary for understanding the invention under 35 U.S.C. § 113 and MPEP § 601.01(f).

First, Applicant submits that the language of claims 74-84 is clear on its face and no illustration or drawing of the claimed biosensor is needed. Thus, claim 74 is drawn to an implantable physiological or pathophysiological biosensor comprising: in vitro or ex vivo

modified stem cells that can be coupled via an electrical interface to endogenous tissue or cells, wherein the in vitro or ex vivo modified stem cells can be implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject, and wherein the in vitro or ex vivo modified stem cells can monitor a chemical, physiological or pathophysiological variable associated with the physiological or pathophysiological function of the subject and can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor. One of skill in the art would easily understand the scope and meaning of claim 74, as well as the scope and meaning of claims dependent on claim 74.

Second, the application provides a clear description of the claimed biosensors, for example, at page 12, line 5 to page 14, line 29 and in the Examples.

Third, during the two and a half years since this application was filed (on October 21, 2003) and during the entire prosecution of the parent application (filed May 3, 2001, now U.S. Patent 6,650,919), no mention of a need for additional drawings was made by the Patent Office. Accordingly, the application, drawings and claims as filed have been deemed to be sufficiently understandable for examination of the application to date. Moreover, the application leading to U.S. Patent 6,650,919 was sufficiently understandable for examination and issuance of a patent.

Fourth, in view of the rejections under 35 U.S.C. §§102 and 103, the Examiner apparently has a sufficiently good understanding of the claimed invention to perform a prior art search.

Applicant therefore submits that submission of Figure 10 is not needed to understand the claimed invention and requests withdrawal of this objection to the drawings.

§101 Rejection of the Claims

Claims 79-82 were rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter (a human or a human body part). As suggested by the Examiner, claim 79 has been amended to recite that the biosensor is adapted to be implanted or inserted in an animal. Applicant submits that claims 79-82 are directed to statutory subject matter and respectfully requests withdrawal of this rejection.

§102 Rejection of the Claims

Claims 74-76 and 78-83 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by 5,750,376 to Weiss et al. According to the Examiner, Weiss describes in vitro and ex vivo modified stem cells that can be coupled via an electrical interface to endogenous cells and can be implanted within a mammal at a site distant from the natural site for physiological function of the subject..

Claim 74 is directed to an implantable physiological or pathophysiological biosensor comprising: in vitro or ex vivo modified stem cells coupled via an electrical interface to endogenous tissue or cells, wherein the in vitro or ex vivo modified stem cells are adapted to be implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject, and wherein the in vitro or ex vivo modified stem cells can monitor a chemical, physiological or pathophysiological variable associated with the physiological or pathophysiological function of the subject and can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989). To constitute anticipation, the claimed subject matter must be identically disclosed in the prior art. *In re Arkley*, 172 U.S.P.Q. 524 at 526 (C.C.P.A. 1972). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 101 (Fed. Cir. 1991). To overcome the defense of anticipation, "it is only necessary for the patentee to show some tangible difference between the invention and the prior art." *Del Mar Engineering Lab v. Physio-Tronics, Inc.*, 642 F.2d 1167, 1172, (9th Cir. 1981).

Moreover, an anticipation rejection that is based on inherency must be supported by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the teaching of the cited art. *Ex parte Levy*,

17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990); *In re Oelrich*, 666 F.2d 578, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

Applicant submits that Weiss et al. disclose and teach only stem cells. Weiss et al. provide no disclosure or teaching whatsoever on a biosensor that contains such stem cells *and* an electrical interface. In fact, none of the following terms can be found anywhere in the Weiss et al. disclosure: electrical, interface and wire. Also, Weiss et al. provide no disclosure whatsoever that in vitro or ex vivo modified stem cells can or should be coupled via an electrical interface to endogenous tissue or cells.

Moreover, while the Examiner has cited to Weiss et al. at col. 22, lines 56-60 and col. 23, lines 37-45 as allegedly teaching biosensors that be coupled via an electrical interface to endogenous cells and can be implanted into mammalian sites distant from a natural site for physiological function, Applicant finds no such disclosure in Weiss et al. In particular, Weiss et al. at col. 22, lines 56-60 merely states that genetically modified precursor cells can be implanted in the CNS. Weiss et al. at col. 23, lines 37-45 merely states that neural stem cell progeny can be administered to any animal with abnormal neurological or neurodegenerative symptoms. Contrary to the Examiner's allegations, Weiss et al. provides no disclosure or teaching that a stem cell can or should be coupled to an endogenous cell be an electrical interface.

Applicant respectfully requests withdrawal of this rejection of claims74-76 and 78-83 under 35 U.S.C. § 102(b).

§103 Rejection of the Claims

Claim 84 was rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,377,721 to Walt et al. in view of U.S. Patent No. 5,750,376 to Weiss et al.. According to the Examiner, while Walt et al. fail to disclose modified stem cells, Weiss et al. cure this defect. The Examiner further asserts that Walt et al. teach a biosensor array useful for drug screening and which can employ virtually any cell type or size, including stem cells, wherein the biosensor array further includes a tube into which the cells are placed. The Examiner cites the Walt et al. disclosure at col. 9, lines 10-26; col. 10, lines 33-50; col. 12, lines 25-36; and col. 15, lines 13-55 as allegedly supporting the Examiner's contentions that claim 84 is obvious in view of Walt.

Claim 84 depends from claim 83 and defines the device of claim 83 as being at least one of a tube, tubing, catheter, wire, wire leads, or an electronic pacemaker.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine reference teachings. Second, the reference(s) must teach or suggest all the claim limitations. Finally, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed modification and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143. If the cited documents do not teach or suggest all the claim limitations, the rejection is improper.

Applicant submits that several elements are missing from the combination of Walt et al. and Weiss et al. First, neither Walt et al. nor Weiss et al. disclose a biosensor having stem cells coupled via an electrical interface to endogenous tissue or cells, wherein the in vitro or ex vivo modified stem cells are adapted to be implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function.

Instead, Weiss et al. merely discloses stem cells as described above. Walt et al. is limited to disclosure of *in vitro* biosensor arrays that largely consist of cell populations confined to microcavities that are used for studying biologically active materials, in situ environmental monitoring, monitoring bioprocesses and screening libraries of chemicals (see, e.g., Walt et al. Abstract). Nowhere do Walt et al. disclose that the arrays or biosensors can or should be adapted to be implanted into a living organism. In fact, the terms "implant," "surgical" and "surgery" appear nowhere in the Walt et al. disclosure. While Walt et al. do contemplate in situ monitoring of environmental pollutants (see Walt et al. Abstract and, the text of the Walt et al. disclosure plainly discloses that such "in situ" monitoring of the environment is done within the environment – outside of a mammal. In particular, Walt et al. discloses the following under section H, entitled "Biosensor Array Applications":

> Since the selectivity of living cells for such compounds has considerable value and utility in drug screening and analysis of complex biological fluids, a biosensor which makes use of the unique characteristics of living cell populations offers distinct advantages in high throughput screening of combinatorial libraries where hundreds of thousands of candidate pharmaceutical compounds must be evaluated. In addition, such a

> biosensor and sensing method can be utilized for either off-line monitoring of bioprocesses or in situ monitoring of environmental pollutants where the enhanced sensitivity of living cells to their local environment can be exploited. Walt et al., col. 32, lines 10-21.

This test clearly indicates that Walt et al. only disclose and contemplate use of their sensors *in vitro* – outside a mammalian body.

Thus, neither Weiss et al. nor Walt et al. disclose and implantable biosensor, because Weiss et al. teach only stem cells (which are not biosensors used to sense and/or respond to endogenous cells through an electrical interface) and Walt et al. disclose only *in vitro* sensor arrays (that are not adapted to be implanted in a mammal or to sense and/or respond to endogenous cells through an electrical interface to those endogenous cells).

A second element that is missing from the combined teachings of the Weiss et al. and Walt et al. disclosures is the combination of the biosensor of present claim 74 and the device of claim 83. Because claim 84 depends from claim 83, which is turn depends from claim 74, claim 84 embraces both the biosensor and the device. As described above, neither Weiss et al. nor Walt et al. disclose an implantable biosensor with an electrical interface to endogenous cells. In addition, neither Weiss et al. nor Walt et al. disclose that the in vitro or ex vivo modified stem cells of a biosensor are incorporated within a device. Thus, even if Walt et al. disclose that cells can be placed on a substrate (e.g. a tube, See Walt at col. 12, lines 25-36), Walt et al. do not disclose the combination of an implantable biosensor (with an electrical interface to endogenous cells) AND a device.

Thus, even though Weiss et al. disclose stem cells and Walt et al. disclose arrays of cells for detecting chemicals and other materials, the combination of these references still fails to disclose the implantable biosensors with the devices of the invention.

Applicant further submits that there is no suggestion or motivation to modify the references or to combine reference teachings to produce the present invention because there is no recognition in either of Weiss et al. or Walt et al. that biosensor stem cells can or should be implanted at site distal from their normal site of function and still sense the physiological function of the distally located endogenous cells. As described above,

Weiss et al. are limited to disclosure of stem cells that may be introduced into a mammal at the site where the function of the stem cells may be needed. Weiss et al. do not disclose or contemplate placement of such cells at a distance from such a site. Nor do Weiss et al. disclose or contemplate that any device may be needed to augment the function of the stem cells. Instead, Weiss et al. teach that the cells should be introduced where they are needed and that such introduction is an end in itself. Such teachings cannot motivate the skilled artisan to use an electrical interface between implanted stem cells and endogenous cells at a distal location. Similarly, Walt et al. do not disclose or contemplate implantation or placement of any cells in any location whatsoever within a mammal. Hence, the teachings of neither Walt et al. nor Weiss et al. would motivate the skilled artisan to modify these references or even combine these references to produce the invention of claim 84.

Finally, one of skill in the art would not have a reasonable expectation of successfully producing the invention of claim 84 from the combination of Walt et al. and Weiss et al. because at least two elements of the present invention are missing from the combined references.

Applicant respectfully submits that claim 84 is patentable in view of Walt et al. and Weiss et al., and requests withdrawal of this rejection under 35 U.S.C. § 103(a).

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date March 6, 2006

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 6th day of March, 2006.

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